

Prioritization of Anti-SARS-CoV-2 Therapies for the Treatment and Prevention of COVID-19 When There Are Logistical or Supply Constraints

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The COVID-19 Treatment Guidelines Panel (the Panel) has recommended several therapeutic agents for the treatment and prevention of SARS-CoV-2 infection in individuals who are at high risk for progression to severe COVID-19. These anti-SARS-CoV-2 therapeutics are of greatest proven clinical benefit for nonhospitalized patients who have risk factors for progression to severe COVID-19. The risks for progression are substantially higher for those who are not vaccinated or who are vaccinated but not expected to mount an adequate immune response to the vaccine.

The Food and Drug Administration's Emergency Use Authorizations provide a broad list of medical conditions or other factors as criteria for use of anti-SARS-CoV-2 agents as treatment or pre-exposure prophylaxis (PrEP). However, at times throughout the pandemic, increased cases of COVID-19 and the emergence of new variants of concern have resulted in logistical or supply constraints that made it impossible to offer the available therapy to all eligible patients. In those situations, prioritization of therapy for those who would have benefited the most became necessary. The purpose of this section is to provide guidance on which individuals might receive the greatest benefit from anti-SARS-CoV-2 therapeutics for treatment or prevention.

When it becomes necessary to triage patients for receipt of anti-SARS-CoV-2 therapies or preventive strategies, the Panel suggests prioritizing:

- Treatment of COVID-19 in unvaccinated or incompletely vaccinated individuals with clinical risk factors for severe illness and vaccinated individuals who are not expected to mount an adequate immune response (see Immunocompromising Conditions below)
- Use of tixagevimab plus cilgavimab (Evusheld) as PrEP for individuals who are severely immunocompromised over those who are moderately immunocompromised (see Immunocompromising Conditions below)

Prioritization of Patients at Highest Risk of Progression to Severe COVID-19

When logistical or supply constraints limit the availability of anti-SARS-CoV-2 monoclonal antibodies (mAbs) or small-molecule antiviral agents, the Panel recommends that clinicians prioritize their use for patients at highest risk of clinical progression. Providers should use their clinical judgment when prioritizing the use of anti-SARS-CoV-2 mAbs for treatment.

Prioritization schemes should consider how to equitably distribute scarce resources to populations that include individuals who may have less knowledge of or access to these therapies. The availability and distribution of recommended therapies should be monitored to ensure that access to products is equitable.

Patient Prioritization for Treatment

The Panel prioritized the following risk groups for anti-SARS-CoV-2 mAbs and antiviral therapy based on 4 key elements: age, vaccination status, immune status, and clinical risk factors. The groups are listed by tier in descending order of priority.

For a list of risk factors, see the Centers for Disease Control and Prevention (CDC) webpage [Underlying](#)

Medical Conditions Associated With Higher Risk for Severe COVID-19.

Tier	Risk Group
1	<ul style="list-style-type: none">Immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying conditions, regardless of vaccine status (see Immunocompromising Conditions below); <i>or</i>Unvaccinated individuals at the highest risk of severe disease (anyone aged ≥ 75 years or anyone aged ≥ 65 years with additional risk factors).
2	<ul style="list-style-type: none">Unvaccinated individuals not included in Tier 1 who are at risk of severe disease (anyone aged ≥ 65 years or anyone aged < 65 years with clinical risk factors)
3	<ul style="list-style-type: none">Vaccinated individuals at high risk of severe disease (anyone aged ≥ 75 years or anyone aged ≥ 65 years with clinical risk factors) <p>Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients within this tier in this situation should be prioritized for treatment.</p>
4	<ul style="list-style-type: none">Vaccinated individuals at risk of severe disease (anyone aged ≥ 65 years or anyone aged < 65 years with clinical risk factors) <p>Note: Vaccinated individuals who have not received a COVID-19 vaccine booster dose are likely at higher risk for severe disease; patients within this tier in this situation should be prioritized for treatment.</p>

Patient Prioritization for Pre-Exposure Prophylaxis

Tixagevimab plus cilgavimab is authorized for use as SARS-CoV-2 PrEP for individuals who have moderate to severe immunocompromising conditions that may result in an inadequate immune response to COVID-19 vaccination. Unlike anti-SARS-CoV-2 agents used for treatment, tixagevimab plus cilgavimab is not authorized for use in unvaccinated individuals unless full vaccination is not possible due to a history of severe allergic reaction to the COVID-19 vaccine. Generally, unless they are also immunocompromised, individuals who qualify for PrEP because of vaccine allergy or contraindication are less likely to suffer severe consequences from SARS-CoV-2 infection than individuals who are moderately to severely immunocompromised.

Immunocompromising Conditions

The CDC website [COVID-19 Vaccines for Moderately or Severely Immunocompromised People](#) provides a list of moderate or severe immunocompromising conditions.¹

If, because of logistical constraints or supply limitations, anti-SARS-CoV-2 therapies cannot be provided to all individuals who are moderately to severely immunocompromised, the Panel suggests prioritizing their use for patients who are least likely to mount an adequate response to COVID-19 vaccination or SARS-CoV-2 infection and who are at risk for severe outcomes, including (but not limited to) the following populations:

- Patients who are within 1 year of receiving B cell–depleting therapies (e.g., rituximab, ocrelizumab, ofatumumab, alemtuzumab)
- Patients receiving Bruton’s tyrosine kinase inhibitors
- Chimeric antigen receptor T cell recipients
- Post-hematopoietic cell transplant recipients who have chronic graft-versus-host disease or who are taking immunosuppressive medications for another indication
- Patients with hematologic malignancies who are on active therapy
- Lung transplant recipients

- Patients who are within 1 year of receiving a solid organ transplant (other than lung transplant)
- Solid organ transplant recipients who had recent treatment with T cell– or B cell–depleting agents for acute rejection
- Patients with severe combined immunodeficiencies
- Patients with untreated HIV who have CD4 T lymphocyte cell counts <50 cells/mm³

If supplies are extremely limited, the Panel suggests prioritizing those who are more severely immunocompromised and who have additional risk factors for severe disease (as discussed below).

Clinical Risk Factors

Some of the most important risk factors for severe COVID-19 include age (risk increases with each decade after age 50),² cancer, cardiovascular disease, chronic kidney disease, chronic lung disease, diabetes, immunocompromising conditions or receipt of immunosuppressive medications, obesity (i.e., body mass index ≥30), and pregnancy. For a complete list of risk factors, including information on the relative risk of severe disease, see the CDC webpage [Underlying Medical Conditions Associated With Higher Risk for Severe COVID-19](#). Of note, the likelihood of developing severe COVID-19 increases when a person has multiple comorbidities.³

Although the data on risk factors for severe COVID-19 in children are limited, there is substantial overlap between risk factors in children and those identified in adults. Children who are aged <1 year or children with obesity, moderate to severe immunosuppression, or complex chronic disease and medical complexity and dependence on respiratory technology are at substantially increased risk of severe disease.⁴

References

1. Centers for Disease Control and Prevention. COVID-19 vaccines for moderately or severely immunocompromised people. 2022. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html>. Accessed March 16, 2022.
2. Centers for Disease Control and Prevention. COVID-19 risks and vaccine information for older adults. 2021. Available at: <https://www.cdc.gov/aging/covid19/covid19-older-adults.html>. Accessed December 22, 2021.
3. Rosenthal N, Cao Z, Gundrum J, Sianis J, Safo S. Risk factors associated with in-hospital mortality in a U.S. national sample of patients with COVID-19. *JAMA Netw Open*. 2020;3(12):e2029058. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/33301018>.
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